

WHAT IS CLAIMED IS:

1. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

(a) the nucleotide sequence as set forth in any of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, or SEQ ID NO: 35;

(b) the nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-1423;

(c) a nucleotide sequence encoding the polypeptide as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36;

(d) a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of any of (a) - (c); and

(e) a nucleotide sequence complementary to any of (a) - (c).

2. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence encoding a polypeptide which is at least about 70 percent identical to the polypeptide as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36, wherein the encoded polypeptide has an activity of the polypeptide set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36;

(b) a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide sequence as set forth in any of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, or SEQ ID NO: 35, the nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-1423, or (a);

(c) a region of the nucleotide sequence of any of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, or SEQ ID NO: 35, the DNA insert in ATCC Deposit No. PTA-1423, (a), or (b) encoding a polypeptide fragment of at least about 25 amino acid residues, wherein the polypeptide fragment has an activity of the encoded polypeptide as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36, or is antigenic;

(d) a region of the nucleotide sequence of any of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, or SEQ ID NO: 35, the DNA insert in ATCC Deposit No. PTA-1423, or any of (a) - (c) comprising a fragment of at least about 16 nucleotides;

(e) a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of any of (a) - (d); and

(f) a nucleotide sequence complementary to any of (a) - (d).

3. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence encoding a polypeptide as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36 with at least one conservative amino acid substitution, wherein the encoded polypeptide has an activity of the polypeptide set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36;

(b) a nucleotide sequence encoding a polypeptide as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36 with at least one amino acid insertion, wherein the encoded polypeptide has an activity of the polypeptide set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36;

(c) a nucleotide sequence encoding a polypeptide as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36 with at least one amino acid deletion, wherein the encoded polypeptide has an activity of the polypeptide set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36;

(d) a nucleotide sequence encoding a polypeptide as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36 which has a C- and/or N- terminal truncation, wherein the encoded polypeptide has an activity of the polypeptide set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36;

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(e) a nucleotide sequence encoding a polypeptide as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36 with at least one modification selected from the group consisting of amino acid substitutions, amino acid insertions, amino acid deletions, C-terminal truncation, and N-terminal truncation, wherein the encoded polypeptide has an activity of the polypeptide set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36;

(f) a nucleotide sequence of any of (a) - (e) comprising a fragment of at least about 16 nucleotides;

(g) a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of any of (a) - (f); and

(h) a nucleotide sequence complementary to any of (a) - (e).

4. A vector comprising the nucleic acid molecule of any of Claims 1, 2, or 3.

5. A host cell comprising the vector of Claim 4.

6. The host cell of Claim 5 that is a eukaryotic cell.

7. The host cell of Claim 5 that is a prokaryotic cell.

8. A process of producing an IL-1ra-R polypeptide comprising culturing the host cell of Claim 5 under suitable conditions to express the polypeptide, and optionally isolating the polypeptide from the culture.

9. A polypeptide produced by the process of Claim 8.

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10. The process of Claim 8, wherein the nucleic acid molecule comprises promoter DNA other than the promoter DNA for the native IL-1ra-R polypeptide operatively linked to the DNA encoding the IL-1ra-R polypeptide.

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A3

11. The isolated nucleic acid molecule according to Claim 2, wherein the percent identity is determined using a computer program selected from the group consisting of GAP, BLASTN, FASTA, BLASTA, BLASTX, BestFit, and the Smith-Waterman algorithm.

12. A process for determining whether a compound inhibits IL-1ra-R polypeptide activity or IL-1ra-R polypeptide production comprising exposing a cell according to any of Claims 5, 6, or 7 to the compound and measuring IL-1ra-R polypeptide activity or IL-1ra-R polypeptide production in said cell.

13. An isolated polypeptide comprising the amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36; and
- (b) the amino acid sequence encoded by the DNA insert in ATCC Deposit No. PTA-1423.

14. An isolated polypeptide comprising the amino acid sequence selected from the group consisting of:

- (a) an amino acid sequence for an ortholog of any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36;
- (b) an amino acid sequence which is at least about 70 percent identical to the amino acid sequence of any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36, wherein the polypeptide has an activity of the polypeptide set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36;
- (c) a fragment of the amino acid sequence set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36 comprising at least about 25 amino acid residues, wherein the fragment has an activity of the

polypeptide set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36, or is antigenic; and

- (d) an amino acid sequence for an allelic variant or splice variant of the amino acid sequence as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36, the amino acid sequence encoded by the DNA insert in ATCC Deposit No. PTA-1423, (a), or (b).

15. An isolated polypeptide comprising the amino acid sequence selected from the group consisting of:

- 10 (a) the amino acid sequence as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36 with at least one conservative amino acid substitution, wherein the polypeptide has an activity of the polypeptide set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36;
- 15 (b) the amino acid sequence as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36 with at least one amino acid insertion, wherein the polypeptide has an activity of the polypeptide set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36;
- 20 (c) the amino acid sequence as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36 with at least one amino acid deletion, wherein the polypeptide has an activity of the polypeptide set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36;
- 25 (d) the amino acid sequence as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36 which has a C- and/or N- terminal truncation, wherein the polypeptide has an activity of the polypeptide set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36; and
- 30 (e) the amino acid sequence as set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36 with at least one modification selected from the group consisting of amino acid substitutions, amino acid insertions, amino acid deletions, C-terminal truncation, and N-terminal truncation,

wherein the polypeptide has an activity of the polypeptide set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36.

16. An isolated polypeptide encoded by the nucleic acid molecule of  
5 any of Claims 1, 2, or 3, wherein the polypeptide has an activity of the polypeptide set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36.

17. The isolated polypeptide according to Claim 14, wherein the  
10 percent identity is determined using a computer program selected from the group consisting of GAP, BLASTP, FASTA, BLASTA, BLASTX, BestFit, and the Smith-Waterman algorithm.

18. A selective binding agent or fragment thereof which specifically  
15 binds the polypeptide of any of Claims 13, 14, 15, 55, or 56.

19. The selective binding agent or fragment thereof of Claim 18 that  
specifically binds the polypeptide comprising the amino acid sequence as set forth  
in any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36, or a  
20 fragment thereof.

20. The selective binding agent of Claim 18 that is an antibody or  
fragment thereof.

21. The selective binding agent of Claim 18 that is a humanized  
25 antibody.

22. The selective binding agent of Claim 18 that is a human antibody  
or fragment thereof.  
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23. The selective binding agent of Claim 18 that is a polyclonal antibody or fragment thereof.

24. The selective binding agent Claim 18 that is a monoclonal  
5 antibody or fragment thereof.

25. The selective binding agent of Claim 18 that is a chimeric antibody or fragment thereof.

10 26. The selective binding agent of Claim 18 that is a CDR-grafted antibody or fragment thereof.

27. The selective binding agent of Claim 18 that is an antiidiotypic antibody or fragment thereof.

15 28. The selective binding agent of Claim 18 that is a variable region fragment.

29. The variable region fragment of Claim 28 that is a Fab or a Fab'  
20 fragment.

30. A selective binding agent or fragment thereof comprising at least one complementarity determining region with specificity for a polypeptide having the amino acid sequence of any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6,  
25 or SEQ ID NO: 36.

31. The selective binding agent of Claim 18 that is bound to a detectable label.

30 32. The selective binding agent of Claim 18 that antagonizes IL-1ra-R polypeptide biological activity.

33. A method for treating, preventing, or ameliorating an IL-1ra-R polypeptide-related disease, condition, or disorder comprising administering to a patient an effective amount of a selective binding agent according to Claim 18.

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34. A selective binding agent produced by immunizing an animal with a polypeptide comprising an amino acid sequence of any of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 36.

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35. A hybridoma which produces a selective binding agent which is capable of binding a polypeptide according to any of Claims 1, 2, or 3.

36. A method of detecting or quantitating the amount of IL-1ra-R polypeptide using the anti-IL-1ra-R antibody or fragment of Claim 18.

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37. A composition comprising the polypeptide of any of Claims 13, 14, 15, 55, or 56, and a pharmaceutically acceptable formulation agent.

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38. The composition of Claim 37, wherein the pharmaceutically acceptable formulation agent is a carrier, adjuvant, solubilizer, stabilizer, or antioxidant.

39. A polypeptide comprising a derivative of the polypeptide of any of Claims 13, 14, 15, 55, or 56.

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40. The polypeptide of Claim 39 that is covalently modified with a water-soluble polymer.

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41. The polypeptide of Claim 40, wherein the water-soluble polymer is selected from the group consisting of polyethylene glycol, monomethoxy-polyethylene glycol, dextran, cellulose, poly-(N-vinyl pyrrolidone) polyethylene



glycol, propylene glycol homopolymers, polypropylene oxide/ethylene oxide copolymers, polyoxyethylated polyols, and polyvinyl alcohol.

42. A composition comprising a nucleic acid molecule of any of  
5 Claims 1, 2, or 3 and a pharmaceutically acceptable formulation agent.

43. The composition of Claim 42, wherein said nucleic acid molecule is contained in a viral vector.

10 44. A viral vector comprising a nucleic acid molecule of any of Claims 1, 2, or 3.

45. A fusion polypeptide comprising the polypeptide of any of Claims 13, 14, 15, 55, or 56 fused to a heterologous amino acid sequence.

46. The fusion polypeptide of Claim 45, wherein the heterologous amino acid sequence is an IgG constant domain or fragment thereof.

47. A method for treating, preventing, or ameliorating a medical  
20 condition comprising administering to a patient the polypeptide of any of Claims 13, 14, 15, 55, or 56, or the polypeptide encoded by the nucleic acid of any of Claims 1, 2, or 3.

48. A method of diagnosing a pathological condition or a susceptibility  
25 to a pathological condition in a subject comprising:

(a) determining the presence or amount of expression of the polypeptide of any of Claims 13, 14, 15, 55, or 56, or the polypeptide encoded by the nucleic acid molecule of any of Claims 1, 2, or 3 in a sample; and

(b) diagnosing a pathological condition or a susceptibility to a  
30 pathological condition based on the presence or amount of expression of the polypeptide.

49. A device, comprising:

(a) a membrane suitable for implantation; and

5 (b) cells encapsulated within said membrane, wherein said cells secrete a protein of any of Claims 13, 14, 15, 55, or 56; and said membrane is permeable to said protein and impermeable to materials detrimental to said cells.

50. A method of identifying a compound which binds to an IL-1ra-R polypeptide comprising:

10 (a) contacting the polypeptide of any of Claims 13, 14, 15, 55, or 56 with a compound; and

(b) determining the extent of binding of the IL-1ra-R polypeptide to the compound.

15 51. The method of Claim 50, further comprising determining the activity of the polypeptide when bound to the compound.

52. A method of modulating levels of a polypeptide in an animal comprising administering to the animal the nucleic acid molecule of any of Claims 1, 2, or 3.

53. A transgenic non-human mammal comprising the nucleic acid molecule of any of Claims 1, 2, or 3.

25 54. A process for determining whether a compound inhibits IL-1ra-R polypeptide activity or IL-1ra-R polypeptide production comprising exposing a transgenic mammal according to Claim 53 to the compound, and measuring IL-1ra-R polypeptide activity or IL-1ra-R polypeptide production in said mammal.

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55. An isolated polypeptide comprising the amino acid sequence as set forth in either SEQ ID NO: 1 or SEQ ID NO: 3 with at least one amino acid substitution selected from the group consisting of: arginine at position 2; alanine, lysine, or arginine at position 3; serine at position 7; lysine at position 8; alanine, cysteine, lysine, threonine, or serine at position 9; cysteine or phenylalanine at position 10; arginine or trptophan at position 13; serine at position 15; arginine at position 18; serine or threonine at position 19; threonine at position 21; serine at position 23; arginine at position 34; tyrosine, serine, or arginine at position 37; lysine, arginine, threonine, or serine at position 38; threonine at position 41; serine, phenylalanine, or alanine at position 43; alanine at position 44; serine or lysine at position 48; alanine, threonine, or phenylalanine at position 52; serine at position 53; serine at position 54; alanine or tyrosine at position 58; lysine at position 65; phenylalanine at position 66; tyrosine at position 67; serine, tyrosine, or phenylalanine at position 69; lysine or serine at position 73; threonine or arginine at position 78; serine or alanine at position 90; alanine at position 91; serine at position 96; lysine or arginine at position 97; lysine or serine at position 98; alanine at position 100; tyrosine at position 102; arginine or alanine at position 104; lysine at position 105; threonine at position 106; arginine at position 108; lysine, threonine, or trptophan at position 109; threonine or serine at position 110; serine at position 111; serine at position 114; serine at position 116; phenylalanine, cysteine, or tyrosine at position 117; tyrosine at position 121; serine or alanine at position 123; cysteine, serine, or threonine at position 126; serine at position 136; phenylalanine or arginine at position 138; threonine, arginine, or alanine at position 141; lysine or tyrosine at position 142; trptophan or threonine at position 143; alanine at position 145; threonine or serine at position 147; cysteine at position 151; and serine, cysteine, or phenylalanine at position 152; wherein the polypeptide has an activity of the polypeptide set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6.

56. An isolated polypeptide comprising the amino acid sequence as set forth in SEQ ID NO: 5 with at least one amino acid substitution selected from the

group consisting of: arginine at position 21; alanine, lysine, or arginine at position 22; serine at position 26; lysine at position 27; alanine, cysteine, lysine, threonine, or serine at position 28; cysteine or phenylalanine at position 29; arginine or trptophan at position 32; serine at position 34; arginine at position 37; serine or  
5 threonine at position 38; threonine at position 40; serine at position 42; arginine at position 53; tyrosine, serine, or arginine at position 56; lysine, arginine, threonine, or serine at position 57; threonine at position 60; serine, phenylalanine, or alanine at position 62; alanine at position 63; serine or lysine at position 67; alanine, threonine, or phenylalanine at position 71; serine at position 72; serine at position  
10 73; alanine or tyrosine at position 77; lysine at position 84; phenylalanine at position 85; tyrosine at position 86; serine, tyrosine, or phenylalanine at position 88; lysine or serine at position 92; threonine or arginine at position 97; serine or alanine at position 109; alanine at position 110; serine at position 115; lysine or arginine at position 116; lysine or serine at position 117; alanine at position 119;  
15 tyrosine at position 121; arginine or alanine at position 123; lysine at position 124; threonine at position 125; arginine at position 127; lysine, threonine, or trptophan at position 128; threonine or serine at position 129; serine at position 130; serine at position 133; serine at position 135; phenylalanine, cysteine, or tyrosine at position 136; tyrosine at position 140; serine or alanine at position 142;  
20 cysteine, serine, or threonine at position 145; serine at position 155; phenylalanine or arginine at position 157; threonine, arginine, or alanine at position 160; lysine or tyrosine at position 161; trptophan or threonine at position 162; alanine at position 164; threonine or serine at position 166; cysteine at position 170; and serine, cysteine, or phenylalanine at position 171; wherein the polypeptide has an  
25 activity of the polypeptide set forth in any of SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6.